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Resolving DNA-ligand intercalation in the entropic stretching regime ALI A. ALMAQWASHI, King Abdulaziz University — Single molecule studies of DNA intercalation are typically conducted by applying stretching forces to obtain force-dependent DNA elongation measurements. The zero-force properties of DNA intercalation are determined by equilibrium and kinetic force-analysis. However, the applied stretching forces that are above the entropic regime (>5 pN) prevent DNA-DNA contact which may eliminate competitive DNA-ligand interactions. In particular, it is noted that cationic mono-intercalators investigated by single molecule force spectroscopy are mostly found to intercalate DNA with single rate, while bulk studies reported additional slower rates. Here, a proposed framework quantifies DNA intercalation by cationic ligands in competition with relatively rapid kinetic DNA-ligand aggregation. At a constant applied force in the entropic stretching regime, the analysis illustrates that DNA intercalation would be measurably optimized only within a narrow range of low ligand concentrations. As DNA intercalators are considered for potential DNA-targeted therapeutics, this analysis provides insights in tuning ligand concertation to maximize therapeutics efficiency.

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